22.7

The Cartilage Autograft Implantation System (CAIS) is being investigated in the US as a primary surgical treatment of articular cartilage lesion(s) located on the femur (medial and lateral condyles or trochlea).

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Purpose: The Cartilage Autograft Implantation System (CAIS) is being investigated as a primary surgical treatment of articular cartilage lesion(s) located on the femur (medial and lateral condyles or trochlea). CAIS involves preparation and delivery of a minced, autologous cartilage tissue-loaded scaffold the site of cartilage lesion(s)' site within a single surgical procedure. This study is designed to assess safety and initial performance.
Methods and Materials: Disposable instruments consisting of an arthroscopic device for harvesting and mincing cartilage tissue, dispersing unit, resorbable scaffold and staples, were developed and optimized. This multicenter, randomized, pilot clinical study (6 sites) may enroll up to 30 subjects. Subjects are randomized in a 2:1 schema (CAIS: microfracture (control) procedure). Subjects return for follow-up at 1 and 3 weeks, 2, 3, 6, 9 and 12 months post-operatively. Subjects are clinically evaluated and interviewed regarding the occurrence of adverse events and asked to complete questionnaires regarding disability, function, pain and quality of life. MRI are completed at baseline, 3 weeks, 6 and 12 months.
Results: In vitro studies show efficient harvest of viable tissue with potential outgrowth performance equivalent to previously published methods. Safety and performance of both clinical study arms will be reported through 6-months.
Conclusions: The instrumentation enabled the successful preparation and fixation of a minced autologous cartilage tissue loaded implant in an intraoperative setting. CAIS device has demonstrated short-term safety in subjects treated to-date. Additional data must be analyzed regarding longer term safety and device performance.

23.3

Mechanical stimulation and hyaluronic acid synergistically enhance remodeling and chondrogenic differentiation of three-dimensional collagen-based construct containing human synovium-derived stem cell

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Purpose: To evaluate the effect of mechanical stimulation and hyaluronic acid on the remodeling and chondrogenic differentiation of three-dimensional construct containing human synovium-derived stem cells.
Methods and Materials: Human knee synovium was digested and librated cells were subcultured for 6 passages. These cells were used to build a three-dimensional construct with collagen gel and a collagen porous scaffold. Cyclic load (0.5Hz, 5 or 20 kPa, 1 hr/day) was applied to the construct with or without hyaluronic acid (1mg/ml). After 5 or 15 days of culture, histological sections, mRNA expression levels and DNA amount of the constructs (n=3 each) were analyzed. Concentration of hyaluronic acid and glycosaminoglycan of cultured media were also measured.
Results: Cyclic load stimulation with hyaluronic acid caused cell aggregation and extracellular matrix accumulation within the pericellular space in the three dimensional constructs. Real-time RT-PCR revealed that cyclic loading of 20 kPa increased aggrecan and Sox 9 mRNA expressions up to 270% and 150% respectively, whereas 5 kPa loading had no effect. Hyaluronic acid synergistically increased these mRNA expressions up to 500% and 150% in 5 kPa and 700% and 240% in 20 kPa respectively. Cyclic loading also upregulated MMP-1, -3 mRNA expressions. CD44, TGF-b1 and HAS 2 mRNA expressions were upregulated by hyaluronic acid under cyclic load stimulation. Concentration of hyaluronic acid and glycosaminoglycan also increased by hyaluronic acid and mechanical stiulation.
Conclusions: Mechanical stimulation and hyaluronic acid synergistically enhance remodeling and chondrogenic differentiation of three-dimensional collagen-based construct containing human synovium-derived stem cells.

23.4

The combination of dynamic compression and shear with rvBMP-2 for in-vitro cartilage tissue engineering

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Purpose: Both bioreactor conditions and gene therapy have shown to enhance chondrogenesis. The purpose of this study was to compare the effects of dynamic compression and shear, alone or in combination with retrovirally expressed bone morphogenetic protein 2 (BMP-2), on chondrocytes in vitro.
Methods and Materials: Primary bovine chondrocytes were either retrovirally transduced with BMP-2 or left untreated. Cells were seeded in 3-D polyurethane scaffolds (n=48) and further cultured under static conditions or exposed to defined dynamic compression and shear in a joint specific bioreactor. One week after seeding four groups were investigated: G1-uninfected, G2-BMP2-infected, G3-uninfected + load and G4-BMP2-infected + load, each at three time points (d7, d21, d35). Outcome measurements included wet weight, DNA-content, glycosaminoglycan (GAG) medium release/scaffold content, collagen 1, 2, aggrecan, Sox 9 mRNA, histology and ELISA for BMP-2-transgene expression. Values given are normalized to G1 at d35.
Results: Wet weight/DNA-content were highest in G4/G2, while DNA-content declined over time. GAG release/scaffold content and GAG per DNA increased over time and was highest in G4/G3 ($p<0,05$). Collagen 1 was lowest in G1/G4, collagen 2 was highest in G4/G2 ($p<0,05$), aggrecan was highest in G3/G4 ($p<0,05$), while Sox9 was highest in G4/G3 ($p>0,05$). Only collagen 2/aggrecan showed significant increases in all groups over time. Cumulation was highest in G4. Histology revealed highest cell density in G4/G2. BMP-2-transgene expression was stable through d35.
Conclusions: When compared to control, in-vitro chondrogenesis is most efficient when simultaneous stimulation with dynamic compression and shear, combined with BMP-2, is applied.

23.5

The mechanical properties of the articular cartilage in second-look after mosaicplasty

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Purpose: We developed an ultrasonic measurement system to detect cartilage stiffness, surface roughness and thickness. The objective of this study was to evaluate the mechanical properties of the grafted cartilage (P), surrounding normal-like cartilage (N), the gap (G) and the donor (D) in second-look after mosaicplasty using our ultrasonic device.
Methods and Materials: There were 22 patients 24 knees who had second-look arthroscopy after mosaicplasty, and we received their informed consent about this study. They were 8 men 14 women, 8 right knees 16 left ones. Their mean operative age in second-look was 47.4 year-old. The mean period from mosaicplasty to second-look was 17.1 months. The number of measured areas was 73 in P, 34 in G and 42 in D. The ratio of the mechanical properties in P, G and D to the ones in N was calculated.
Results: In stiffness, P (106.2%) was significantly larger than G (49.3%) and D (65.1%). In surface roughness, P (93.2%) was significantly smaller than G (113.8%) and D (107.9%). In thickness, there was no significant. In the mechanical properties of P, there was significant difference in only stiffness among the period from mosaicplasty to second-look. The ratio of stiffness in P was 58.4% in less than 6 months, 99.1% in from 11 to 16 months and 204.7% in more than 22 months.
Conclusions: At second-look, the grafted plugs had similar mechanical properties as normal after 1 year. However, the stiffness in P was larger than the stiffness in surrounding normal-like cartilage after 2 years.